

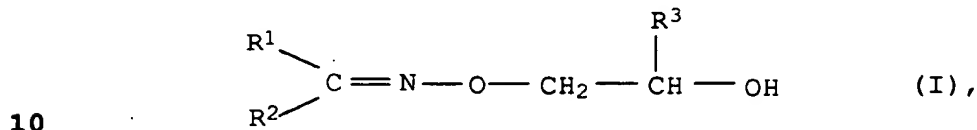
28 Rec'd PCT/PTO 03 FEB 1997

Preparation of O-(2-hydroxyalkyl) Oximes

This application is a 371 of PCT/EP95/03001 filed 28 Feb 1995.

The present invention relates to a process for the preparation of

5 O-(2-hydroxyalkyl) oximes of the general formula I



in which R¹ and R² each stand for an alkyl group having from 1 to 10 carbon atoms, or form, together with the carbon atom to which they are attached, a 5-membered to 7-membered cycloalkyl radical, 15 and R³ denotes an alkyl group having from 1 to 10 carbon atoms.

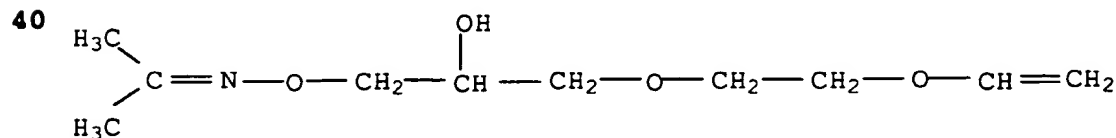
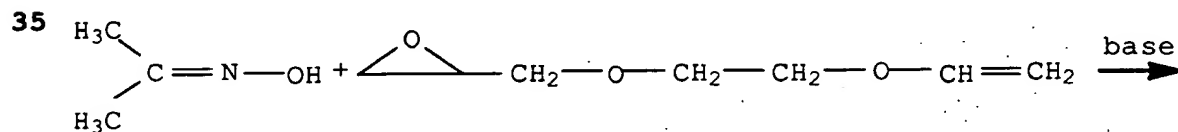
O-(2-hydroxyalkyl) oximes have great significance as intermediates for plant protectants (cf eg, the prior German Application DE-A 44 15 887).

20

J. Amer. Chem. Soc., 81, pp 4223 to 4225 (1959) and US-A 3,040,097 describe a process for the preparation of O-(2-hydroxy-alkyl)-oximes in which the parent oximes are caused to react with olefin oxides under basic conditions, in particular in the pres- 25 ence of alkali metal bases.

PL-A 53,525 (Chemical Abstracts, 68, 491 75d (1968)) reveals that tertiary amines are suitable bases for a similar case.

30 Specially substituted O-hydroxyalkyloximes can be prepared by the reaction of 25 glycol vinyl glycidyl ethers with oximes in the presence of bases such as triethylamine or potassium hydroxide, for example.



45

(cf. Zh. Org. Khim., 23, 1426 to 1429 (1987)).

Furthermore, it is well known that it is possible to cause reaction of acetone oxime with ethylene carbonate in toluene in the presence of potassium fluoride to produce O-(2-hydroxyethyl)acetone oxime (cf. Amer. Chem. Soc. Symposium Series 443 page 231(1991)).

Furthermore, a process for the preparation of bis[O-(2-hydroxyethyl)dimethyl-glyoxime starting from dimethylglyoxime and ethylene carbonate is described in J. Polymer Sci., 10, page 3408 (1972).

In accordance with the earlier application EP-A 655,437, aldoximes and ketoximes with unsubstituted or C₁-C₈-alkyl-substituted ethylene or propylene carbonate can be hydroxyalkylated in the presence of catalytic amounts of an N-alkylated, stable organic base or of pyridine substituted by a secondary amine.

It was the object of the invention to provide a more economical process for the preparation of O-(2-hydroxyalkyl)oximes I.

Accordingly, we have found a process for the preparation of O-(2-hydroxyalkyl)-oximes of the formula I, wherein a ketoxime of the formula II



is caused to react with

a) an olefin oxide of the formula III

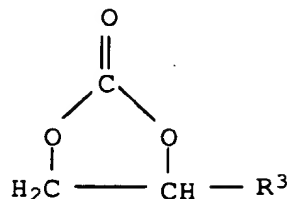


in the presence of a tertiary amine or

3

b) a carbonate of the formula IV

5



(IV),

10 in the presence of a catalyst.

The reaction of II with a carbonate IV is preferred.

The following literature citations "Houben-Weyl" refer to Houben-
15 Weyl, Methoden der Organischen Chemie, 4th ed., Thieme Verlag, Stuttgart.

Preferred process products I are those which can be produced by this process variant those are preferred in which R¹ and R² stand
20 for c₁-c₄ alkyl groups and primarily c₁-c₃ alkyl groups or form, together with the carbon atom to which they are attached, a cyclopentyl or cyclohexyl ring, and in particular those in which R¹ and R² stand for methyl and/or ethyl or form, together with the carbon atom to which they are attached, cyclohexyl. R³ preferably
25 stands for a c₁-c₄ alkyl group, particularly for ethyl and more particularly for methyl. Most particularly preferred compounds I are those in which R¹, R² and R³ stand for methyl.

The ketoximes II are generally known or are obtainable by known
30 methods, for example, by the reaction of the corresponding ketones with hydroxylamine.

The olefin oxides III are also generally known or are obtainable by known methods.

35

The carbonates IV are also generally known or can be produced by known methods (cf. eg, EP-A 543,249).

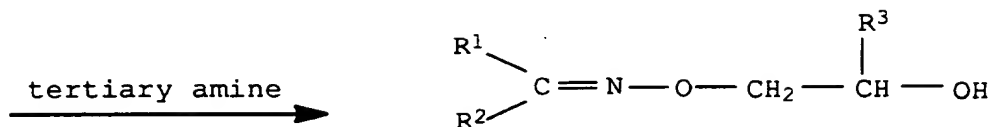
(a) Reaction of ketoximes II with olefin oxides III in the pres-
40 ence of a tertiary amine:

45

4



5



10

The molar ratio of olefin oxide III to ketoxime II is preferably from 1:1 to 2:1 and in particular from 1.1:1 to 1.3:1.

Suitable tertiary amines, either alone or in the form of a mixture, are primarily those having aliphatic and/or cycloaliphatic groups on the N atom such as triethylamine, tri-n-propylamine, tri-n-butylamine, tri-n-octylamine, tri-n-dodecylamine, N-methyldicyclohexylamine, and N,N-dimethylcyclohexylamine and also heterocyclic nitrogen bases having from 5 to 10 carbon atoms such as pyridine, 4-(N,N-dimethylamino)pyridine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,4-diaza-bicyclo[2.2.2]octane, and 1-methylimidazole.

Preferably, with regard to the fact that the reaction mixture present at the end of the reaction is to be subjected to purification by distillation, a tertiary aliphatic amine is used whose boiling point is between 50° and 250°C and in particular between 80° and 180°C. Triethylamine and N,N-dimethylcyclohexylamine are particularly preferred.

30

The tertiary amine is usually employed in an amount of from 0.5 to 40 mol%, preferably from 0.9 to 10 mol% and more preferably from 1 to 5 mol%, based on the ketoxime II.

The reaction can be carried out without the use of solvent or in a suitable solvent or solvent mixture.

Suitable solvents are alkanols such as ethanol and tert-butanol, ethers such as 1,4-dioxane and tetrahydrofuran, ketones such as acetone, esters such as ethyl acetate, nitriles such as acetonitrile, N,N-dialkylamides such as dimethyl formamide and N,N-dimethylacetamide, N-alkylated lactams such as N-methyl-2-pyrrolidone, and N,N-dialkylated cyclic ureas such as N,N-dimethylethylene urea and N,N-dimethylpropylene urea.

45

5

Also suitable as solvent is an excess of one of the aforementioned tertiary amines which is in the liquid state at least under the reaction conditions.

- 5 From a process engineering point of view, those of the aforementioned solvents are preferred, broadly speaking, which have a similar boiling point to that of the amines used and/or form azeotropes with them such that their removal, by distillation, from the crude reaction mixture takes place in a particularly
10 simple manner.

Particularly preferred are the N,N-dialkylamides and N-alkylated lactams, especially dimethylformamide and N-methyl-2-pyrrolidone.

- 15 There are usually employed from 50 to 500 mL and preferably from 50 to 200 mL of solvent, based on 1 mol of the ketoxime II.

- The reaction is carried out at temperatures of from 40° to 130°C and mostly from 70° to 110°C and pressures of from 0.5 to 40 bar
20 and mainly from standard pressure to 20 bar.

- Preferably the process is carried out by placing the ketoxime II and the tertiary amine, optionally in a solvent, in the reactor and metering in the olefin oxide III at the temperature of
25 reaction.

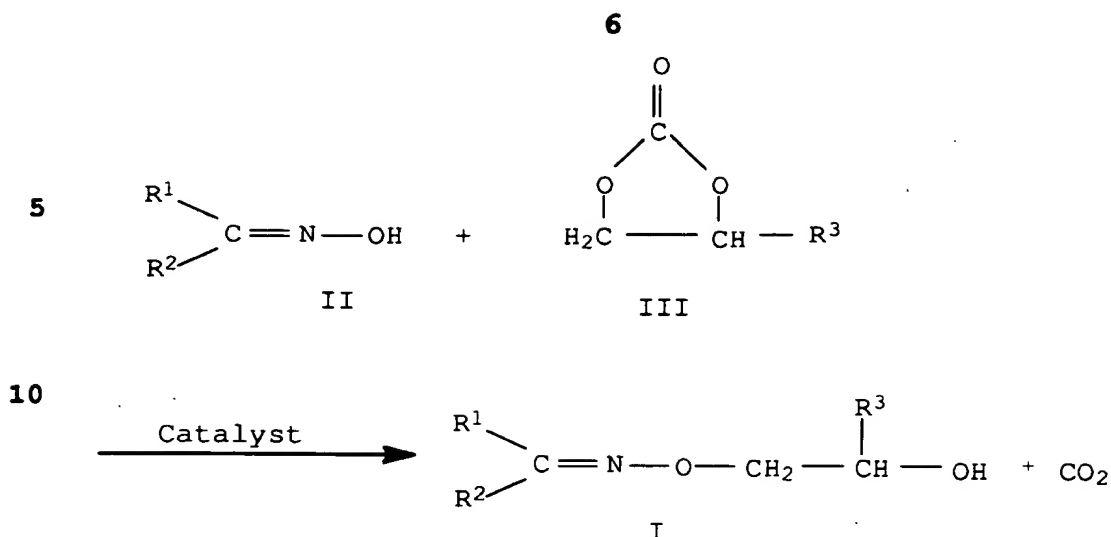
The reaction times are normally from 2 to 24 h but mostly from 4 to 16 h.

- 30 The isolation of the reaction products I takes place by methods known per se, preferably by distillation.

- (b) Reaction of ketoximes II with carbonates IV in the presence of a catalyst:
35

40

45



15

The molar ratio of carbonate IV to ketoxime II is usually from 1:1 to 10:1 and in particular from 4:1 to 7:1.

Suitable catalysts, used either alone or in the form of a mixture, are

20 a) alkali metal salts, alkaline earth metal salts, and ammonium salts (NN₄⁺), primarily the potassium salts and also the sodium salts' with inorganic or organic anions such as alkali metal halides, hydroxides, carbonates, hydrogen carbonates, alcoholates, and alkali metal salts of organic monocarboxylic acids. By way of example, there may be mentioned potassium fluoride, potassium iodide, potassium hydroxide, potassium carbonate, potassium hydrogen carbonate, potassium methylete, potassium ethylete, potassium tertbutylete, and potassium acetate;

35 b) ammonium salts and preferably phosphonium salts having at least one organic group in the cation and containing inorganic or organic anions, primarily the halides, hydrogen carbonates, and acetates of such phosphonium salts in particular those containing three c₁-c₄ alkyl and/or phenyl groups, such as tri-n-butylphosphonium acetate and triphenylphosphonium chloride;

40

45 c) phosphines having at least one but preferably three c-organic radicals, in particular those selected from the group comprising c₁-c₁₀ alkyl, c₆-c₁₅-aryl, c₆-c₁₅ alkylaryl, and/or c₇-c₁₀-arylalkyl, such as, primarily tri-n-butylphosphine and triphenylphosphine; or

- 5 δ) tertiary amines, preferably heterocyclics having from one to three N atoms as hetero atoms, such as, primarily, imidazoles, particularly N-(C₁-C₄ alkyl)imidazoles such as N-methylimidazole, and also triazoles, pyridines, and bicyclic azaheterocyclics such as 1,8-diazabicyclo[5.4.0]undec-7-ene and 1,4-diazabicyclo[2.2.2]octane.

Preferred catalysts are those which are mentioned under (α) and (δ). Of the (α) group, the potassium salts are preferably used, especially potassium fluoride or potassium hydrogen carbonate. Of the (δ) group, triethylamine is most particularly preferred.

The catalyst, primarily the inorganic alkali metal salts and the alkali metal salts of carboxylic acids, can be bonded to a support, if desired. Examples of suitable supports are aluminum oxide, silica gel, and kieselguhr. The amount of catalyst in these supported catalysts is usually from 10 to 50 wt%.

The catalysts are usually employed in an amount of from 5 to 50 mol%, preferably from 5 to 30 mol%, and more preferably from 5 to 10 mol%, based on the ketoxime II.

The reaction can be carried out in a single, preferably aprotic, organic solvent or in a solvent mixture. However, the process is preferably carried out without the use of a solvent, in which case an excess of the carbonate IV can, in particular, serve as reaction medium.

Suitable solvents are for example alkylbenzenes, such as, in particular, toluene and also the xylenes, furthermore dialkylketones such as methyl ethyl ketone, halobenzenes such as chlorobenzene, and ethers such as 1,4-dioxane.

The amount of solvent used is usually from 1 to 9 times and in particular from 2 to 7 times the weight of the ketoxime II. If the amount of solvent exceeds 9 times the weight of the ketoxime II, conversion and yield usually fall.

The reaction is preferably carried out at temperatures of from 80°C to 150°C and mostly from 100°C to 140°C and pressures of from 0.5 to 1 bar and especially under standard pressure.

The addition of a conventional phase transfer catalyst usually leads to an increase in reaction rate and conversion. However, for simple processing, it is preferred not to use a phase transfer catalyst.

Examples of phase transfer catalysts are quaternary ammonium or phosphonium salts, preferably tetraalkylammonium, tetraalkylphosphonium, trialkylbenzylammonium, or trialkylbenzylphosphonium salts, especially triethylammonium, tributylbenzylammonium, and
5 tetrabutylammonium chlorides, bromides, and hydrogen sulfates, and also tributylhexaphosphonium bromide.

The phase transfer catalyst is usually employed in an amount of from 0.5 to 2 mol% and preferably from 0.7 to 1 mol%, based on
10 the ketoxime II.

The reaction can be carried out batchwise or, preferably, continuously.

15 The reaction times are normally from 8 to 24 h but mostly from 8 to 16 h.

The isolation of the reaction product I takes place by methods known per se, preferably by distillation.

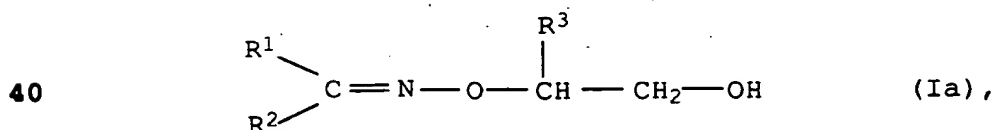
20

The distillation residues of the crude mixture contain substantially unconverted carbonate JV and the catalyst.

In a preferred embodiment of the process of the invention the
25 process is carried out by replenishing the ketoxime II and the carbonate IV at a rate equal to the rate of consumption thereof, following the distillation of the product I from the reaction mixture, and the reaction is then repeated.

30 It has been found that in up to 20 successive reactions carried out in this manner in the same reactor, the yield of the compound I falls inappreciably and the ratio of the isomers I and Ia remains approximately the same.

35 The reaction frequently also produces, as by-product, the regioisomeric compound Ia



which is usually obtained in amounts of up to 10 %, based on I. The two isomeric compounds I and Ia are normally the first over-
45 heads occurring during distillation of the crude product. If desired, the isomer Ia can be substantially separated from the

compound I by methods known per se, preferably by fractional distillation.

The end products I are important intermediates for crop protection agents, especially for herbicides of the cyclohexenone type (cf. DE-A 44 15 887).

Examples

10 Example 1

Preparation of O-(2-hydroxypropyl)propane-2-one oxime (II + III according to (a))

- 15 2.92 kg (40 mol) of acetone oxime were dissolved in 5.2 L of dimethyl formamide and admixed with 0.2 kg (2 mol) of triethylamine. This mixture was heated to 70°C in an autoclave well purged with nitrogen gas. Over a period of 4 h, 2.56 kg (44 mol) of propylene oxide were metered in at this temperature, and on
- 20 completion of the addition, the reaction was allowed to continue for a further 3 h at 70°C. The autoclave was then depressurized, and unconverted propylene oxide was extensively removed at 200 mbar and 70°C, by distillation.
- 25 During purification, by distillation, of the crude mixture with the aid of a column having a length of 50 cm and a diameter of 5 cm and packed with 3 mm V₂A gauze rings, 2.84 kg of a mixture of O-(2-hydroxypropyl)propane-2-one oxime and O-(2-hydroxy-1-methylethyl)propan-2-one oxime were obtained at 78-81°C/30 mbar of. The
- 30 percentage isomer ratio I:Ia determined by gas chromatography was 96:4.

Example 2

- 35 Preparation of O-(2-hydroxybutyl)propan-2-one oxime (II + III according to (a))

Example 1 was repeated except that butylene-1 oxide was used instead of propylene oxide. During fractional distillation of the

40 crude product, a mixture of O-(2-hydroxybutyl)propan-2-one oxime and O-(2-hydroxy-1-ethylethyl)propan-2-one oxime was obtained at 80-82°C/20 mbar in a yield of 59 %. The isomer ratio of I:Ia was 96.7:3.3.

Example 3

Preparation of O-(2-hydroxypropyl)cyclohexanone oxime (II + III according to (α))

5

Example 1 was repeated starting from cyclohexanone oxime instead of acetone oxime. During fractional distillation of the crude product a mixture of O-(2-hydroxypropyl)cyclohexanone oxime and O-(2-hydroxy-1-methylethyl)cyclohexanone oxime was obtained at 10 74°C/0.2 mbar in a yield of 54 %. The isomer ratio of I:Ia was 96:4.

Example 4

15 Preparation of O-(2-hydroxypropyl)propanone oxime (II + IV according to (β))

585 g (8 mol) of acetone oxime, 4080g (40 mol) of propylene carbonate, and 80 g (0.8 mol) of potassium hydrogen carbonate in 20 200g of toluene were caused to react for a period of 8 h at 130°C. There followed fractional distillation of the reaction mixture. The fraction of desired product consisting of O-(2-hydroxypropyl)propane-2-one oxime and O-(2-hydroxy-1-methylethyl)propan-2-one oxime distilled over at 70- 75°C/20-30 mbar in 25 a percentage ratio of I:Ia of 92:8.

Following cooling of the distillation residues, toluene, acetone oxime, and propylene carbonate were replenished to the aforementioned quantities and the reaction was then repeated. Follow- 30 ing further 10 reactions of the type just described, an average was taken over all 12 reactions. The yield of O-(2-hydroxyalkyl) oximes was found to be 90 % based on acetone oxime.

Example 5

35

Preparation of O-(2-hydroxypropyl)propanone oxime (II + IV according to (β).)

The process was carried out as in Example 4 but without the addition of toluene. Starting from 344 g (4.7 mol) of acetone oxime, 40 2420 g (23.5 mol) of propylene carbonate, and 47 g (0.47 mol) of potassium hydrogen carbonate there was obtained, in a total of 10 reaction cycles carried out, in each case, for a period of 8 h at 130°C, a mixture consisting of O-(2-hydroxypropyl)propane-2-one 45 oxime and O-(2-hydroxy-1-methylethyl)propane-2-one oxime in a percentage ratio of I:Ia of 92:8 and in a yield of 89%.

Example 6

Preparation of O-(2-hydroxypropyl)propanone oxime
(II + IV according to (β))

5

The process was carried out as in Example 4 but with the addition of 1086 g of toluene. Starting from 585 g (8 mol) of acetone oxime, 2450 g (24 mol) of propylene carbonate, and 80 g (0.8 mol) of potassium hydrogen carbonate there was obtained, in a total of 10 5 reaction cycles carried out, in each case over a period of 8 h at 125-130°C, a mixture consisting of O-(2-hydroxypropyl)propane-2-one oxime and O-(2-hydroxy-1-methylethyl)propan-2-one oxime in a percentage ratio of I:Ia of 92:8 and at a yield of 89 %.

15

Example 7

Preparation of O-(2-hydroxypropyl)propane-2-one oxime
(II + IV according to (β))

20

292.5 g (4.0 mol) of acetone oxime, 2040 g (20 mol) of propylene carbonate and 100 g (1.0 mol) of triethylamine were introduced into a stirred apparatus and stirred at an oil bath temperature of 130°C for 8 hours. After cooling, distillation was carried out 25 (bubble-cap tray column, 60 cm long, 30 mm in diameter). 80 g of triethylamine was recovered. The distillation residue, which consisted to the extent of 90% of unconsumed propylene carbonate, was able to be used for the next reaction with acetone oxime.

30 Yield (b.p. 9 mbar = 46°C): 85%.

35

40

45